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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/697,329 10/27/00 IISHI

E 1422-449F

EXAMINER

HM22/0214

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HABTE, K
ART UNIT

PAPER NUMBER

1624
DATE MAILED:

02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/697,329

Applicant(s)

IISHI ET AL.

Examiner

Kahsay Habte, Ph. D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 7 is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8-11 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claims ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

Specification

1. The specification on page 1 (line 4) provides information about the status of this application as "continuation-in-part of PCT/JP00/4835", but on the preliminary amendment letter sent on October 27, 2000 refers to this application as "continuation application of PCT/JP00/4835". Correction or clarification is required.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-9 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kaspersen *et al.* {Journal of Label. comp. and Radiopharm., 27, No. 9, 1055 (1989)}. Kaspersen *et al.* teaches the multi-step synthesis of Org-3770 (mirtazapine) on page 1058 (Fig.4). On page 1066, Kaspersen *et al.* teaches the synthesis of mirtazapine and the crystallization of the mirtazapine (compound **1c**) from the crude product using methanol/water solvent mixture to achieve almost pure crystals. Compound **1c** is ¹³carbon labelled product, but since the claim embraces the labelled compounds, the crystals product acquired from this process are identical to the claimed crystals of mirtazapine. The synthesis of compound **1d** on page 1067 also can be used as an

problem
for
preparing
crystals
of mirtazapine

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additional prior art, even though Kaspersen *et al.* did not provide any information on the specific nature of the product (solid, crystal, or oily). Since compound **1c** and **1d** are the same compounds, therefore compound **1d** is also presumed to be crystal. These products (crystals from compound **1c**) including compound **1d**, are exactly the same compounds (crystals of mirtazapine) claimed by the applicants.

3. Claims 1 and 2 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kaspersen *et al.* {Journal of Label. comp. and Radiopharm., 27, No. 9, 1055 (1989)}. Kaspersen *et al.* teaches the multi-step synthesis of Org-3770 (mirtazapine) on page 1058 (Fig.4). On page 1066, Kaspersen *et al.* also teaches the crystallization of the mirtazapine from the crude product using methanol/water solvent mixture to achieve almost pure crystals. Claims 1 and 2 are product claims, in which applicants recite some of the physical and chemical characteristics of the said product. Since reference (Kaspersen *et al.*) teaches the crystallization method essentially the same as applicants, it is reasonable to presume that products would or should have same characteristics. In re Wiegand 86 USPQ 155, 158; In re Zelinski 141 USPQ 217; Ex parte Fryling 115 USPQ 99.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaspersen *et al.* Kaspersen *et al.* on page 1066 teaches crystallization of mirtazapine crude product from methanol/water to achieve colorless crystals. Applicants recite in claim 10 the preparation of crystals by dissolving the crude mirtazapine in water-soluble organic solvent and thereafter by adding water. Applicants also recite in claim 11, the same procedure as in claim 10, but using heat (adjusting the temperature).

Kaspersen *et al.* (on page 1066) teaches a crystallization method from methanol/water that is identical to the applicants, even though it is not explicitly outlined on how it was carried out. One in skilled in the art will understand that crystallization of mirtazapine product from methanol/water involves one of these methods: (1) dissolving of the mirtazapine product in a heated methanol/water solvent, and then cooling the resulting solution (same as claim 11) or (2) dissolving of the mirtazapine product in a water soluble organic solvent (such as methanol), and thereafter by adding water (same as claim 10). Since Kaspersen *et al.* teaches the crystallization of the mirtazapine product using methanol/water, it is obvious at the time of the invention was made to the person having ordinary skill in the art to understand that crystallization of mirtazapine product can be carried out by either said methods.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 3, the phrase "comprising drying the crystals" is unclear. It is not clear when the drying takes place? Is drying takes place while the crystals are stored or it takes place after storage?

6. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 1 and 3, the phrase "hygroscopic degree of not more than 0.6%" is unclear. It is not clear what hygroscopic degree is. What does it indicate?

7. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 8, the phrase "comprising crystallizing a crude mirtazapine using a water-soluble organic solvent and water" is indefinite. There are three ways that the claim could be understood:

a. by dissolving crude mirtazapine in a minimum amount of water-soluble organic solvent, and thereafter adding water.

b. by dissolving crude mirtazapine in a heated water-soluble organic solvent, and thereafter allow the resulting solution to cool down in an ice bath.

c. by dissolving crude mirtazapine in a minimum amount of water, and thereafter by adding water-soluble organic solvent.

It is not clear if claim 8 is referring to method a, b, or c.

8. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 11, the phrase "temperature of the solution to 0° to 30°C" is confusing. It is not clear what "to 0° to 30°C" is referring to. Does it include temperature ranges between 0° to 30°C or just 0° and 30°C only? Does this mean heating from 0° to 30°C?

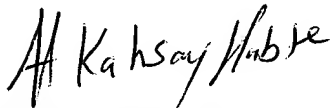
Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte, Ph. D. whose telephone number is (703) 308-4717. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Kahsay Habte, Ph. D.
Examiner
Art Unit 1624



Mark L. Berch
Primary Examiner
Art Unit 1624

KH
February 7, 2001